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Organic and Coordination Chemistry of 1,2,4-Trithiolanes

GrzegorzMlostoń,*[a] Jarosław Romański,[a] Wolfgang Weigand,[b] and Heinz Heimgartner [c]

Dedicated to Professor Naomichi Furukawa on the occasion of this 82nd birthday

Abstract: The review is aimed in summarizing the most important aspects of the chemistry of 1,2,4- trithiolanes, which form a relevant class of cyclic polysulfides abundant in nature. Some of them were identified as components of *Lenthinus edodes* (shiitaki mushrooms) extracts as well as of *Parkia speciosa* (stink bean), which are well known as delicious food-stuff in cuisine of some Asian countries. In addition, they determine the flavour of boiled beef and roasted chicken meet. Thermal decomposition of 1,2,4-trithiolanes, either in solution or in the gas phase, results in [3+2]-cycloelimination leading to the release of reactive thiocarbonyl *S*-sulfides existing in equilibrium with sulfur-rich, three-membered dithiiranes. Both, 1,2,4-trithiolanes and the products of their decomposition react with low-valent platinum and iron compounds forming the corresponding sulfur-metal complexes. For example, iron-sulfur clusters formed in these reactions are of interest as structural models of [Fe,Fe]-hydrogenase mimics.

Grzegorz Mlostoń completed chemistry studies at the University of Łódź (Poland) and subsequently prepared the Ph.D. thesis entitled 'Reactions of Phenylmethylene with Imines' under supervision of Prof. R. Bartnik. In the period 1983-1998 he spent several post-doctoral stays abroad working in the groups of Prof. R. Huisgen (Munich), G. Maier (Giessen), H. Heimgartner (Zurich), G. A. Olah (Los Angeles), and H.-U. Reissig (Berlin). Currently he occupies the full-professor position at the University of Łódź (since 1998). In the period 2012-2016 he served the academic community as the Dean of the Faculty of Chemistry. He was awarded the Liebig Lecturship by the German Chemical Society (2012), Kostanecki's, and Śniadecki's Medals by the Polish Chemical Society (2013). His research interest is focused on modern organic synthesis, heteroatom chemistry, fluorine organic chemistry, reactive intermediates, organic reaction mechanisms, asymmetric synthesis, and related problems.

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Wolfgang Weigand received his PhD degree from the LMU of Munich under the supervision of W. Beck in 1986. After a postdoctoral stay with D. Seebach at ETH Zurich, he finished his Habilitation at the LMU in 1994. Since 1997 he is Professor of Inorganic Chemistry at the Friedrich Schiller University Jena (Thuringia). He has received the "Thuringian Research Prize 2003" and the Medal of Honor "The University of Lodz (Poland) in Service of Science and Society". In 2016 he was chair of the 27th International Symposium on the Organic Chemistry of Sulfur (ISOCS-27).

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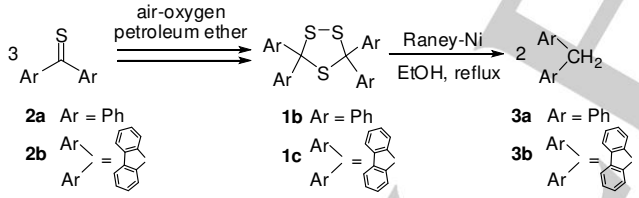
Privatdozent in 1980, Titular professor in 1987, and in 1995 he was appointed Associate Professor. Since 2006 he is Emeritus Professor. He was awarded the Werner Medal and Prize of the Swiss Chemical Society in 1978, the Medal "In Service of Science and Society" of the University of Lodz in 2001, the Honorary Membership of the Polish Chemical Society in 2002, the Kametani Award in 2005, the Team Prize 2007 of the Polish Ministry of Science and Higher Education, the Doctor Honoris Causa of the University of Lodz in 2009, and the Professor Honoris Causa of the State University St. Petersburg in 2010. His research activities range from organic photochemistry and mechanisms of organic reactions to the preparation of heterocyclic compounds and the synthesis and conformation of sterically crowded peptides.

1. Introduction

Among the five-membered sulfur-rich heterocycles, alkyl- and aryl-substituted derivatives of 1,2,4-trithiolane (**1a**, Figure 1) form an important class of compounds, which formally can be attributed to cyclic polysulfides. The first reports related to the synthesis of first representatives concerned the conversions of thiobenzophenone (**2a**) into 3,3,5,5-tetraphenyl-1,2,4-trithiolane (**1b**) upon exposure to air-oxygen[1] or-by treatment with 3,4,5,6-tetrachloro-*o*-quinone at 2 °C.[2] In analogy to the better known 1,2,4-trioxolanes ('secondary ozonides'), they used to be named as 'thioozonides'. The correctness of the postulated structure was proved by treatment of **1b** with Raney-Ni, which led to diphenylmethane (**3a**) as the sole product. An analogous structure **1c** was attributed to the product obtained after mild oxidation of thiofluorenone (**2b**).[3]



Scheme 1. Formation of 1,2,4-trithiolanes **1b**,**c** by treatment of aromatic thioketones **2a**,**b** with air-oxygen.

There is a growing interest in the chemistry of 1,2,4-trithiolanes and their oxides as many derivatives are widely spread in the nature. In addition, they are important components of enzymatic or thermal decomposition of food components. For example, Shiitake mushrooms (*Lentinusedodes*) are known to contain diverse cyclic polysulfides, and the parent 1,2,4-trithiolane (**1a**, Figure 1) is identified as one of the major components.[4] It was also found as the major cyclic polysulfide in stink bean (*Parkiaspeciosa)* as the source of H_2S, which is slowly released as the product of its enzymatic decomposition.[5] Some 3,5-dialkyl-substituted 1,2,4-trithiolanes, e.g. *cis*-and *trans*-3,5-diethyl-1,2,4-trithiolanes (**1d**), were detected as components of volatile oils isolated from flowers and leaves of *Allium cepa*[6] as well as from some natural essential oils.[7] The isomeric 1- and 4-oxides of **1a**, i. e. compounds **4a** and **4b**, respectively, which display anti-cancer activity, were isolated from the red alga *Chondriacalifornica*[8] (Figure 1).

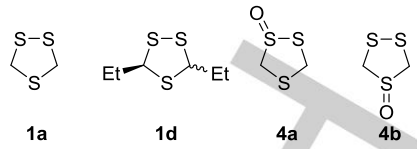


Figure 1. The parent 1,2,4-trithiolane (**1a**) and some of its derivatives isolated from natural sources.

Thermal degradation of some α-amino acids as components of proteins produces complex mixtures of volatile organosulfur compounds including 3,5-dialkyl-1,2,4-trithiolanes. For example, they are responsible for the flavor of beef broth[9] and roasted chicken.[10]

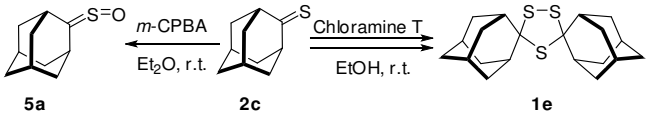
In the last three decades, we witnessed a remarkable development of the chemistry of 1,2,4-trithiolanes. On the one hand, they have been applied as a unique source of reactive thiocarbonyl *S*-sulfides useful for the preparation of diverse sulfur heterocycles via [3+2]-cycloaddition, and on the other one, they react with thiophilic platinum and iron complexes to give sulfur heterocyclic metal complexes. These aspects are in the focus of the present review covering basically reports from the last two decades.

2. Methods for the preparation of 1,2,4-trithiolanes

As mentioned in the introduction, the oldest method for the synthesis of 3,3,5,5-tetraaryl-1,2,4-trithiolanes is the air-oxygen-mediated conversion of the corresponding aromatic thioketones, which is applicable only for the symmetrically substituted derivatives.[1–3] This approach is still of preparative value. However, new oxidizing agents have been applied to improve the efficiency and the scope of this procedure.

2.1.Oxidation of aromatic and cycloaliphatic thioketones

Oxidation of thiobenzophenone (**2a**) with tetrachloro-*o*-quinone in a ratio of 1:3 in ether afforded the 1,2,4-trithiolane **1b** in 73% yield.[11] Chloramine T was also applied as an efficient oxidizing agent for the conversion of both aromatic thioketones and adamantanethione (**2c**) to give the corresponding symmetric 1,2,4-trithiolanes.[12] In contrast to **2c**, which delivered **1e** in 37% yield (Scheme 2), the enolizablethiocamphor was converted under these conditions into the disulfide derived from its enethiol form.[12]

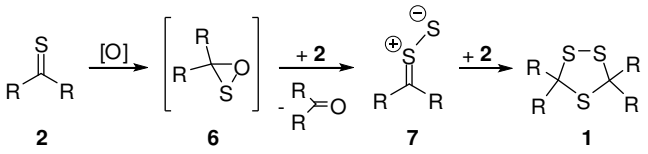


Scheme 2. Oxidations of adamantanethione (**2c**) with Chloramine T or with *m*-CPBA.

It is worth mentioning that the oxidation of **2c** with *m*-CPBA affords adamantanethione *S*-oxide (sulfine**5a**), which is a stable compound at ambient conditions[13] and reacts as 1,3-dipole with thioketones yielding regioselectively 1,2,4-oxadithiolanes as products of the [3+2]-cycloaddition.[13c]

The detailed reaction mechanism, which governs the transformations of non-enolizable thioketones into 1,2,4-trithiolanes, is unknown. However, the intermediacy of oxathiiranes **6**[14] as sulfur-donating species and the formation of highly reactive thiocarbonyl *S*-sulfides **7**, via a 'sulfur-transfer

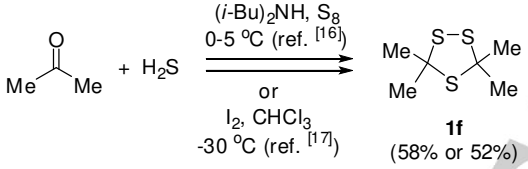
mechanism' are very likely. The latter intermediate undergoes the [3+2]-cycloaddition with the starting thioketone **2**, yielding the final cycloadduct **1** (Scheme 3).



Scheme 3. Oxathiiranes **6** as *S*-transferring intermediates in transformations of thioketones**2** into 1,2,4-trithiolanes **1**.

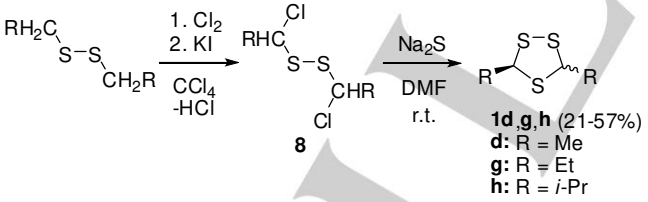
2.2. Conversion of carbonyl compounds with hydrogen sulfide

Enolizable ketones and aldehydes can be converted efficiently into the corresponding alkylated 1,2,4-trithiolanes using Asinger's method, which consists in the treatment of the carbonyl compounds with H_2S, secondary amines, and elemental sulfur.[15,16a] In the case of aldehydes, mixtures of *cis*- and *trans*-3,5-dialkyl-1,2,4-trithiolanes are formed.
Another procedure for the synthesis of tetraalkyl- but also 3,5-dialkyl-3,5-diaryl-1,2,4-trithiolanes is based on the treatment of the respective ketones with H_2S in the presence of I_2 in chloroform solution[17] (Scheme 4).



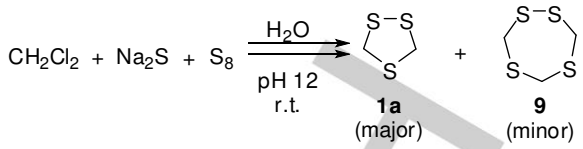
Scheme 4. Conversion of acetone into 3,3,5,5-tetramethyl-1,2,4-trithiolane (**1f**) by treatment with hydrogen sulfide.

An alternative method for the preparation of 3,5-dialkyl-1,2,4-trithiolanes is the chlorination of a dialkyl disulfide in CCl_4 followed by treatment of the intermediate α,α'-dichlorodialkyl disulfides**8** with Na_2S in DMF at room temperature[16a] (Scheme 5).



Scheme 5. Cyclization of α,α'-dichlorodialkyl disulfides**8** by treatment with Na_2S.

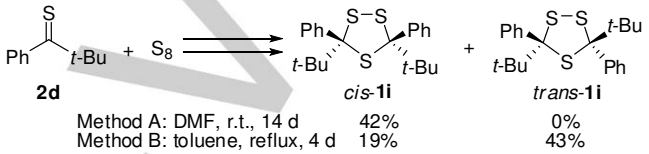
In a very recent report, formation of **1d** from ethyl acetate and gaseous products obtained after thermal decomposition of thiourea was described.[16b]
Asinger's method cannot be applied for the preparation of the parent 1,2,4-trithiolane (**1a**). Instead, the two-phase reaction of dichloromethane (CH_2Cl_2) with a mixture of $Na_2S{\cdot}9H_2O$ and S_8 in water at room temperature leads to **1a** along with 1,2,4,6-tetrathiepane (**9**)[4a] (Scheme 6).



Scheme 6. Formation of the parent 1,2,4-trithiolane (**1a**) in the two-phase reaction of CH_2Cl_2/H_2O with Na_2S/S_8.

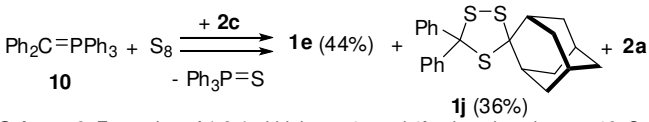
2.3. Reactions of thioketones with elemental sulfur

Elemental sulfur was used to convert *tert*-butyl phenyl thioketone (**2d**) into the isomeric tetrasubstituted 1,2,4-trithiolanes **1i**. Whereas the reaction performed in DMF at room temperature (14 days) afforded *cis*-**1i** as the exclusive product, a similar procedure in boiling toluene led after 4 days to a mixture of *trans*-**1i** and *cis*-**1i** in a ratio of 43:19[18] (Scheme 7).



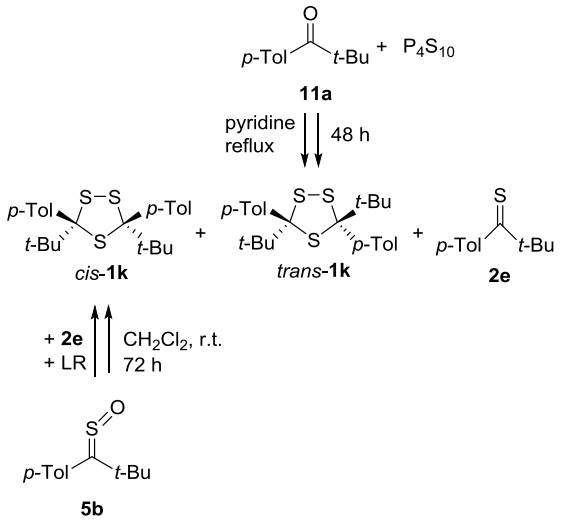
Scheme 7. Reaction of thioketone **2d** with elemental sulfur.

Adamantanethione (**2c**) reacts with S_8 in the presence of NaSPh in boiling acetone to yield, after 15 min, only small amounts of trithiolane **1e** along with the corresponding dispiro-1,2,4,5-tetrathiane, formed as the major product.[19] On the other hand, treatment of **2c** with S_8 in $CHCl_3$ under reflux for 2 days in the presence of a catalytic amount of $Ph_3P{=}S$ led to **1e** in 59% yield.[20] In a similar experiment, the phosphorane**10** was reacted with S_8 in boiling toluene, and subsequent addition of **2c** gave, after 24 h, a mixture of **1e** as the major product and the non-symmetric 1,2,4-trithiolane **1j**[20] (Scheme 8). These products are formed via [3+2]-cycloadditions of the in situ-formed thiocarbonyl *S*-sulfides of type **7** with thioketones **2a** and or **2c** (cf. Scheme 3). However, the symmetric **1a** is known as a thermally labile compound,[11,21] which under the applied conditions undergoes [3+2]-cycloelimination.



Scheme 8. Formation of 1,2,4-trithiolanes **1e** and **1j** using phosphorene **10**, S_8 and adamantanethione (**2c**).

The parent **1a** was found as a component of a mixture of organosulfur compounds formed from CS_2 and oxalic acid under hydrothermal conditions.[4e]
Some ketones, e.g. *tert*-butyl *p*-tolylketone (**11a**), react with P_4S_{10} to yield, after heating in pyridine for 48h, a mixture of *cis*- and *trans*-isomer of the tetrasubstituted 1,2,4-trithiolane **1k** (35% and 13%, resp.), accompanied by the corresponding thioketone **2e** (23%)[22] (Scheme 9). In this case, the initial step is very likely the thionation of **11a** to give **2e**, which via the intermediate thiocarbonyl *S*-sulfide and its [3+2]-cycloaddition with another molecule of **2e** forms the thermostable, isomeric cycloadducts **1k**.

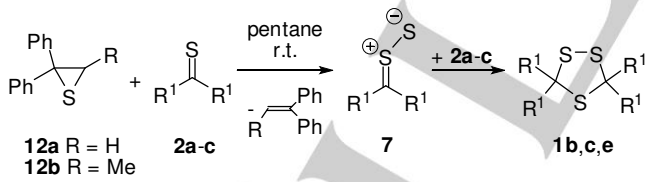


Scheme 9. Synthesis of 1,2,4-trithiolanes **1k** via thionation of ketone **11a** with P_4S_{10} or sulfine **5b** with Lawesson's reagent.

Interestingly, treatment of the sulfine**5b** with Lawesson's reagent (LR) in the presence of thioketone **2e** in CH_2Cl_2 at room temperature results in the formation of *cis*-**1k** as the sole product in 79% yield.[23] On the other hand, the reaction of **2e** with LR at room temperature led to the same product, *cis*-**1k**, in 26% yield, only after much longer reaction time (19 days).

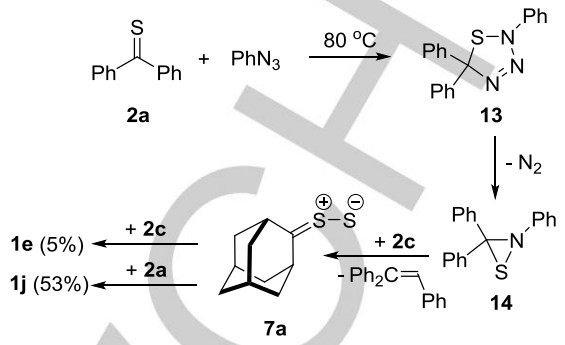
2.4. Sulfur-transfer reactions with usage of thiiranes or in situ-formed thiaziridines

An important method for the preparation of tetrasubstituted 1,2,4-trithiolanes relies on the sulfur-transfer from thiiranes **12a**,**b** to a thioketone **2**, and the intermediate thiocarbonyl *S*-sulfide **7** formed thereby is trapped by another thioketone molecule to yield the corresponding [3+2]-cycloadduct **1**. This method gives excellent yields of symmetric 1,2,4-trithiolanes starting with thiobenzophenone (**2a**), thiofluorenone (**2b**), and adamantanethione (**2c**)[11,21] (Scheme 10). An analogous experiment was also carried out with 4,4-dichlorothiobenzophenone.



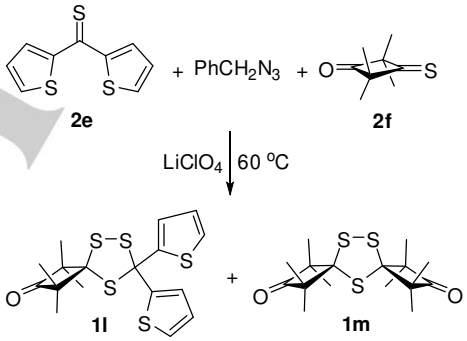
Scheme 10. Preparation of tetrasubstituted symmetric 1,2,4-trithiolanes **1** via sulfur-transfer from thiiranes **12** to thioketones **2**.

Another type of sulfur-transfer reaction leading to tetrasubstituted 1,2,4-trithiolanes is based on thermal reactions of organic azides with thioketones. For example, adamantanethione (**2c**) reacts in a two-component reaction with phenyl azide at 80 °C to afford the symmetrictrithiolane**1e** in 33% yield. The same product was obtained with benzyl azide, butyl azide,[23] and methyl azidoacetate.[24] Similar three-component reactions performed with an aromatic and a cycloaliphatic thioketone, e.g. **2a** and **2c**, dissolved in phenyl azide, led to mixtures of symmetric and non-symmetric tetrasubstituted 1,2,4-trithiolanes, e.g. **1e** and **1j**[23,25,26] (Scheme 11).



Scheme 11. Three-component reaction of a mixture of thioketones **2a** and **2c** dissolved in phenyl azide leading to the 1,2,4-trithiolanes **1e** and **1j**.

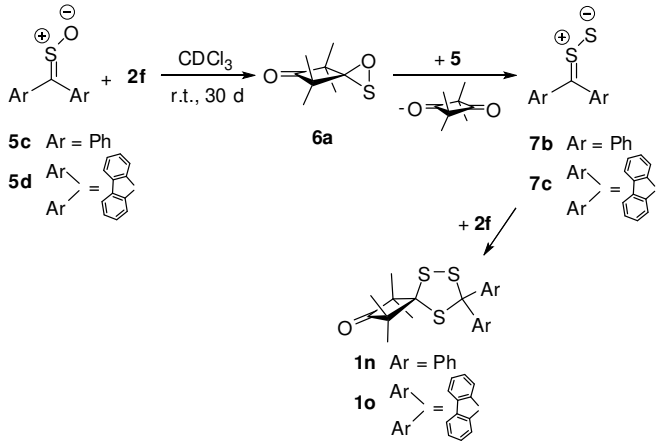
In three-component reactions with some hetaryl thioketones, e.g. di(2-thienyl) thioketone (**2e**), with 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**2f**), and excess benzyl azide, a similar reaction course leads to two types of 1,2,4-trithiolanes **1**, but in this case, $LiClO_4$ was applied as an activator[26] (Scheme 12).



Scheme 12. Three-component formation of non-symmetric and symmetric 1,2,4-trithiolanes **1l** and **1m**.

The formation of 1,2,4-trithiolanes presented in Schemes 11 and 12 is the result of multiple [3+2]-cycloadditions. The initial step consists in the cycloaddition of the azide with the more reactive aromatic thioketone, and the unstable cycloadduct of type **13** is formed. Spontaneous elimination of N_2 leads to thiaziridine**14**, which acts as a S-donor to the C=S group, to generate the transient thiocarbonyl *S*-sulfides of type **7**. The latter undergo the next cycloaddition with unconverted thioketones to yield thermally stable, *spiro*-substituted 1,2,4-trithiolanes.

Non-symmetric 1,2,4-trithiolanes **1n** and **1o** were obtained in multistep reactions between aromatic sulfines**5c**,**d** and monothione**2f**. In these transformations, the last step leading to the 1,2,4-trithiolane skeleton is also a [3+2]-cycloaddition of the intermediate aromatic thiocarbonyl*S*-sulfide onto the C=S group of **2f**[27] (Scheme 13). The reactive 1,3-dipole (*S*-sulfide) is generated via sulfur-transfer from the postulated cycloaliphatic oxathiirane**6a** to the S-atom of the aromatic thioketone. The competitive S-transfer from this intermediate was also studied using thiobenzophenone (**5b**) and (*E*)-cyclooctene as sulfur acceptors.[28]



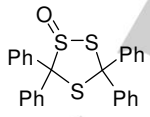
Scheme 13. The postulated oxathiirane **6a** as S-donor in the formation of non-symmetric 1,2,4-trithiolanes **1n** and **1o**.

3. Transformations of 1,2,4-trithiolanes and their *S*-oxides

3.1. Oxidations of 1,2,4-trithiolanes

As mentioned in the introduction, two regioisomeric monoxides **4a** and **4b** derived from the parent 1,2,4-trithiolane (**1a**) were isolated from red algae. An independent synthesis of both compounds was carried out starting with **1a** in acetone, and $NaIO_4$ was used as oxidizing reagent.[6] The obtained mixture of *S*-oxides **4a** and **4b** was separated chromatographically to yield 26% of **4a** and 27% of **4b**, respectively.

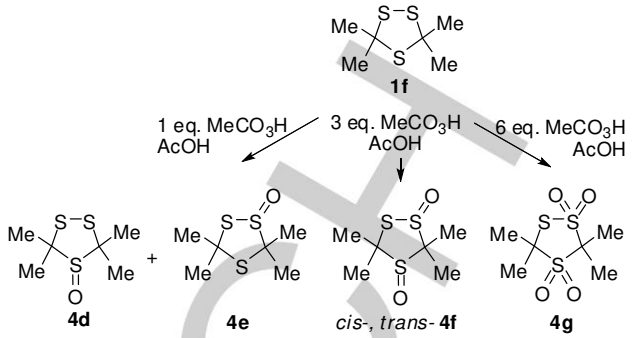
The oxidation of **1a** with *m*-CPBA was also reported. In the reaction carried out with an equimolar amount of *m*-CPBA in dichloromethane, **4a** and **4b** were also formed in comparable amounts.[29a] By using 2.5 mol-equiv. of *m*-CPBA, the *trans*-1,4-dioxide was obtained as the sole product after 24h.[29a] The same method was applied for the preparation of 3,3,5,5-tetraphenyl-1,2,4-trithiolane 1-oxide (**4c**) from **1b**(Figure 2). The crystalline product was isolated in 54% yield, and its structure was confirmed by X-ray diffraction analysis.[29b]



4c

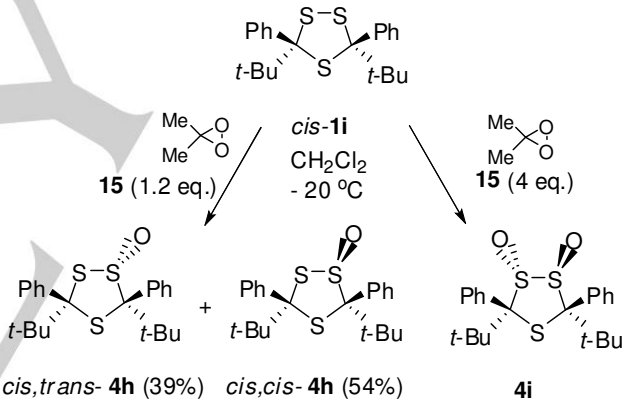
Figure 2. 3,3,5,5-Tetraphenyl-1,2,4-trithiolane 1-oxide (**4c**)

The oxidation with peroxyacetic acid ($MeCO_3H$) was applied in the case of 3,3,5,5-tetramethyl-1,2,4-trithiolane (**1f**), and depending on the molar ratios of substrate and reagent, mixtures of monoxides **4d** and **4e**, *cis*- and *trans*-1,4-dioxides **4f** or tetraoxide **4g** were isolated[29a] (Scheme 14). The structures of oxides *trans*-**4f** and **4g** were proved by X-ray crystallography.



Scheme 14. Oxidation of 3,3,5,5-tetramethyl-1,2,4-trithiolane (**1f**) with peroxyacetic acid.

Oxidations of the sterically crowded 1,2,4-trithiolanes *cis*- and *trans*-**1i** were carried out using dimethyldioxirane (**15**) in CH_2Cl_2 solutions at –20 °C.[18,30] The oxidation of *cis*-**1i** with 1.2 equivalents of **15** gave a 54:39-mixture of isomeric 1-oxides *cis,cis*- and *cis,trans*-**4h** with retention of the configuration of the substituents at C(3) and C(5) and *cis*/*trans* orientation of the O-atom towards the phenyl groups (Scheme 15). The reaction with 4 equivalents of **15** led to the corresponding 1,2-dioxide **4i** with *trans* orientation of the O- atoms.

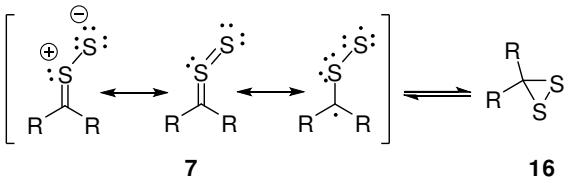


Scheme 15. Oxidation of *cis*-**1i** with varying amounts of dimethyldioxirane (**15**).

An analogous experiment performed with *trans*-**1i** and 1.2-equivalents of **15** afforded also a mixture of two isomeric 1-oxides with preserved configuration of the substituents at C(3) and C(5). Interestingly, further oxidation of one of the isolated isomers with 4 equivalents of **15** led to a mixture of the corresponding 1,2-dioxide (minor) and the 1,1-dioxide (major), whereas the reaction with peroxyacetic acid led to the same products in a reversed ratio.

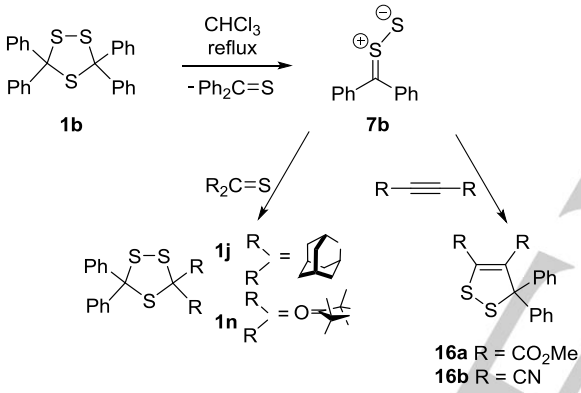
3.2. [3+2]-Cycloeliminations leading to thiocarbonyl *S*-sulfides

Thiocarbonyl*S*-sulfides **7** belong to the class of sulfur-centered 1,3-dipoles and are believed to exist in equilibrium with dithiiranes **16**[31] (Scheme 16). They are known as reactive intermediates and have never been isolated. However, generated in situ they can be trapped with a suitable dipolarophile forming the corresponding five-membered, sulfur rich [3+2]-cycloadduct.



Scheme 16. Mesomeric structures of thiocarbonyl *S*-sulfides **7** and the equilibrium with dithiiranes **16**.

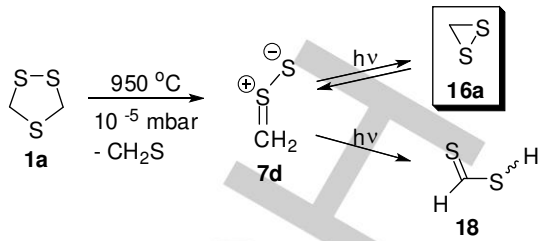
Huisgen and Rapp showed that the thermolabile 3,3,5,5-tetraphenyl-1,2,4-trithiolane (**1b**) is an excellent precursor for the generation of thiobenzophenone *S*-sulfide (**7b**) via thermal [3+2]-cycloelimination.[11,21] A simple procedure relies in the heating of **1b** with a slight excess of the respective dipolarophile in boiling $CHCl_3$.Using this protocol, electron deficient acetylenes were converted into the respective 3*H*-1,2-dithioles **17** (Scheme 17). Trapping of **7a** with cycloaliphatic thioketones **2c** and **2f** leads to the thermally stable non-symmetric 1,2,4-trithiolanes **1j** and **1n**, respectively.[11,27] Analogous [3+2]-cycloadditions are described for the thiocarbonyl *S*-sulfide generated thermally from 3,3,5,5-tetra(4-chlorophenyl)-1,2,4-trithiolane.[11]



Scheme 17. Trapping of thiobenzophenone *S*-sulfide (**7a**) with acetylenic and thiocarbonyl dipolarophiles.

3.3. Gas-phase pyrolysis and first detection of the parent dithiirane

Gas-phase pyrolysis in combination with matrix technique is an excellent method for detection and identification of reactive intermediates and unstable organic compounds. The parent 1,2,4-trithiolane (**1a**) undergoes [3+2]-cycloelimination at 950 °C in vacuum. The obtained products were identified by means of IR-spectroscopy and computational methods, which demonstrated that the major products are thioformaldehyde *S*-sulfide (**7d**) and thioformaldehyde. These products, immobilized in an Ar-matrix at 10 K, were photolyzed, and thereby **7d** was converted initially to the parent dithiirane (**16a**) and subsequently to dithioformic acid (**18**) (existing as a mixture of *s-cis* and *s-trans* rotamers) as products of its photo-isomerization[32] (Scheme 18). This result was confirmed in a very recent study based on application of a more advanced high-level coupled-cluster method.[33]

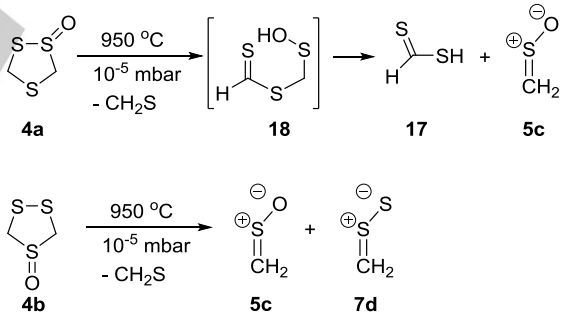


Scheme 18. Gas-phase thermolysis of the parent 1,2,4-trithiolane **1a**; first identification of the parent dithiirane **16a**.

The corresponding dithiiranes **16b** and **16c** (Figure 3) were also detected in Ar-matrices at 10 K after gas-phase pyrolysis of 1,2,4-trithiolanes **1f** and **1m**, respectively .[34]

Figure 3. Substituted dithiiranes **16b** and **16c** isolated in Ar-matrix at 10 K.

Flash vacuum pyrolysis (FVP) of isomeric *S*-oxides of the parent 1,2,4-trithiolane, i.e. **4a**,**4b**, leads to different products. In the case of **4b**, a mixture of thioformaldehyde *S*-oxide (**5c**), *S*-sulfide (**7d**), and thioformaldehyde formed the major part of the pyrolysate collected in Ar-matrix. Under the same conditions, **4a** undergoes fragmentation leading to dithioformic acid (**18**), thioformaldehyde *S*-oxide (**5c**), and thioformaldehyde. In that case, the formation of a substantial amount of dithioformic acid (**18**) was explained by the initial 1,4-H shift followed by ring opening to give **19** as the key intermediate[35] (Scheme 19).



Scheme 19. Vacuum pyrolysis of isomeric *S*-oxides **4a** and **4b** derived from the parent 1,2,4-trithiolane.

4. Coordination chemistry of 1,2,4-trithiolanes

4.1. Reactions with diphosphane Pt(0) complexes

The reaction of 3,3,5,5-tetraphenyl-1,2,4-trithiolane (**1b**) with $(Ph_3P)_2Pt(\eta^2\text{-}C_2H_4)$ was performed in toluene at 0°C, and the reaction course was monitored by ^{31}P NMR spectroscopy.[36] The solid product was identified as a 1:1 mixture of the platinathiirane **20a** and the dithiolato-complex **21a**(Figure 4). In the same study, the latter compound was also prepared in an independent synthesis from thiobenzophenone (**2a**) and $(Ph_3P)_2Pt(\eta^2\text{-}C_2H_4)$.

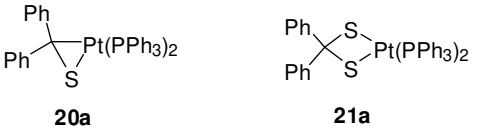
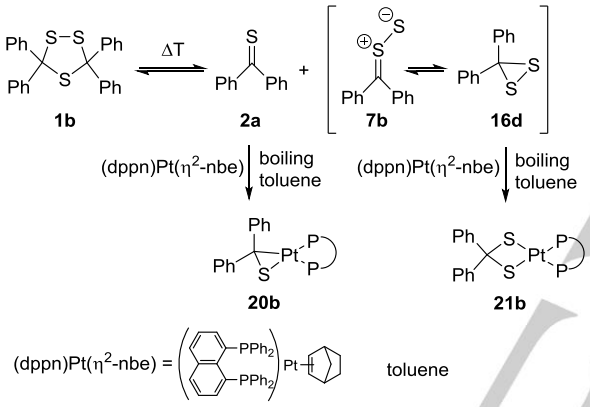


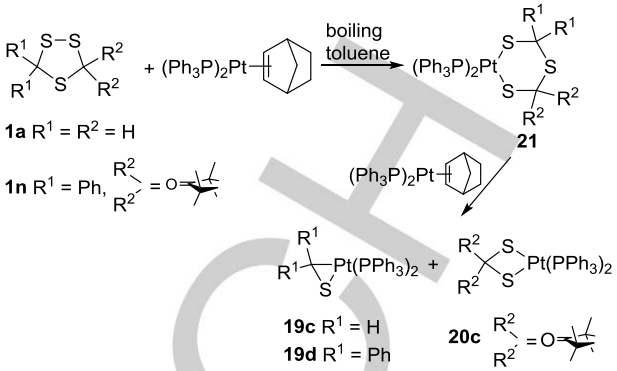
Figure 4. Platinathiirane **20a** and dithiolato-complex **21a** obtained from 3,3,5,5-tetraphenyl-1,2,4-trithiolane (**1b**) and $(PPh_3)_2Pt(\eta^2\text{-}C_2H_4)$.

Analogous products were formed upon treatment of **1b** with other (bisphosphane) Pt(0) complexes bearing 1,8-bis(diphenylphosphanyl)naphthalene (dppn). The reactions with these complexes required higher temperature, and for that reason, the toluene solution was heated to 50 °C[37] (Scheme 20). Under these conditions, the starting **1b** is believed to exist in equilibrium with **2a** and **7b**/**16d**. In this system, the initially formed **7b** undergoes 1,3-dipolar electrocyclization forming dithiirane **16d**. Complexation of the C=S group of **2a** then leads to **20b**, and the oxidative addition of Pt(0)-complex along the S–S bond in **16d** affords the dithiolato-complex **21b**. This interpretation was supported by a kinetic study.[37]



Scheme 20. Mechanistic interpretation of the reaction of **1b** with (dppn)Pt(η^2-nbe) complex.

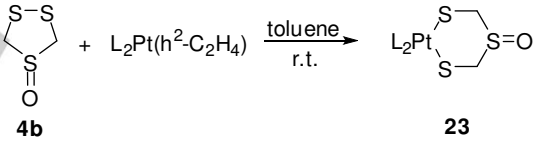
Similar studies performed with differently substituted 1,2,4-trithiolanes demonstrated that the 'dithiirane mechanism' shown in Scheme 20 has to be replaced by the alternative ring-expansion of the starting 1,2,4-trithiolane **1** resulting in the formation of six-membered Pt-heterocycles **22**, which undergo thermal decomposition with release of the corresponding thioketone, which is subsequently trapped by another bisphosphane Pt(0) complex[38,39] (Scheme 21). The postulated six-membered intermediate formed from **1n** and $(Ph_3P)_2Pt(\eta^2$-nbe) is stable at room temperature, and its structure was confirmed not only spectroscopically but also by X-ray crystallography.[39



Scheme 21. Ring-expansion of 1,2,4-trithiolanes **1** leading to the intermediate six-membered Pt-heterocycles **22**.

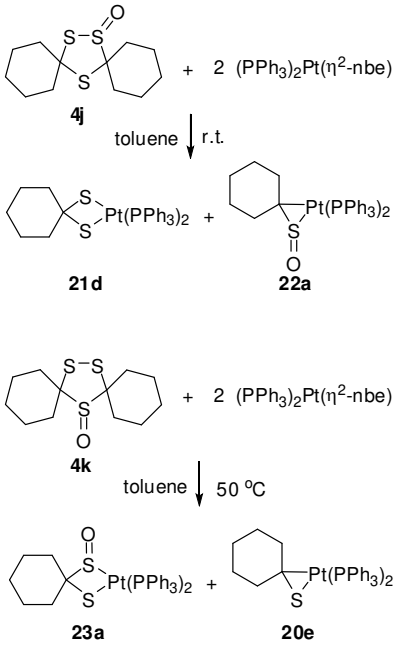
In analogy to 1,2,4-trithiolanes, bisphosphane Pt(0) complexes react also with α,α'-dichloroalkyloligosulfanes prepared from monothioketone**2f** yielding the corresponding platinathiirane of type **20** and the dithiolato Pt(II) complex **21c**. Interestingly, in contrast to **1b**, the sterically crowded 1,2,4-trithiolane **1m** did not react with $(Ph_3P)_2Pt(\eta^2\text{-}C_2H_4)$in toluene at room temperature for 24 h.[40]

In extension of the studies with 1,2,4-trithiolanes, the reactions of their *S*-oxides with bisphosphane Pt(0) complexes ($L_2Pt(0)$) were also studied. Thus, 4-*S*-oxide **4b**, derived from the parent 1,2,4-trithiolane (**1a**), gave stable six-membered Pt-complexes **23**, which were isolated and identified by means of spectroscopic methods. In contrast to the non-oxidized **1a**, a stable product was observed even in the case of L = PPh_3[38] (Scheme 22).



Scheme 22. Ring expansion of 4-*S*-oxide **4b** with Pt(0)-complexes (L = PPh_3).

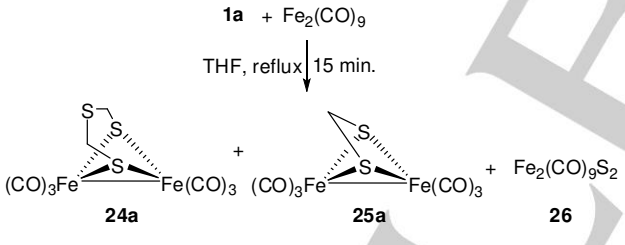
The dispirocyclic1,2,4-trithiolane *S*-oxides **4j** and **4k** were reacted with $(Ph_3P)_2Pt(\eta^2$-nbe), and in contrast to **4b**, products **21d**, **22a**, and **23a**, **20e**, respectively, resulting from the decomposition of the intermediate of type **22**, were isolated[41] (Scheme 23).



Scheme 23. Splitting of isomeric 2-*S*- and 4-*S*-oxides **4j** and **4k** in reactions with $(Ph_3P)_2Pt(\eta^2\text{-nbe})$ complex.

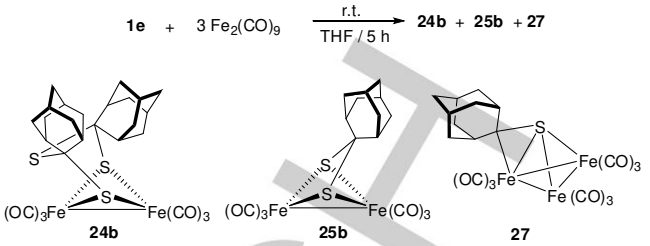
4.2. Reactions with iron carbonyls

Reactions of differently substituted 1,2,4-trithiolanes with $Fe_2(CO)_9$ or $Fe_3(CO)_{12}$ have also been studied. Thus, the parent **1a** reacts with $Fe_2(CO)_9$ in boiling THF solution yielding the complex **24a** as the major product (38%). In addition, products **25a** and **26** were also found in the reaction mixture[42] (Scheme 24).



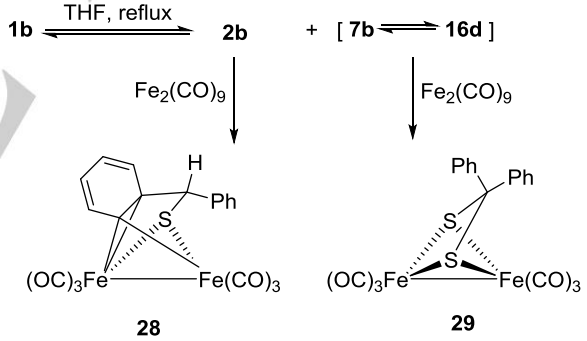
Scheme 24. Reactions of $Fe_2(CO)_9$ with the parent 1,2,4-trithiolane **1a**.

Whereas compound **24a** is formed via insertion along the sulfur-sulfur bond of **1a**, the mechanism leading to **25a** upon formal elimination of thioformaldehyde(H_2C=S), is still unknown. Analogous products were obtained starting with three equivalents of $Fe_2(CO)_9$ in reactions with 3,3,5,5-tetraalkyl-substituted 1,2,4-trithiolanes **1f** and **1o**.[43] However, in the case of the dispiro-substituted 1,2,4-trithiolane **1e**, the reaction mixture contained products **24b** and **25b** along with the complex **27**, containing adamantanethione (**2c**) side-on coordinated with the $Fe_3(CO)_9$ cluster[43] (Scheme 25). Apparently, the formation of the latter results from the release of adamantanethione (**2c**) after thermal [3+2]-cycloelimination of the starting **1e**.



Scheme 25. Three products **24b**, **25b** and **27** formed in the reaction of $Fe_2(CO)_9$ with sterically crowded dispiro substituted 1,2,4-trithiolane **1e**.

As pointed out in Chapter 3.2, symmetric 3,3,5,5-tetraaryl-1,2,4-trithiolanes are thermolabile compounds and undergo easily the [3+2]-cycloelimination. For that reason, the reactions with iron carbonyls ($Fe_2(CO)_9$ and $Fe_3(CO)_{12}$) performed under enhanced temperature comprise the complexation of aromatic thioketones and aromatic thiocarbonyl *S*-sulfides existing in an equilibrium with the corresponding dithiiranes. The first reaction with the aromatic thioketone followed by 1,3-H shift leads to the bimetallic complex **28** containing σ as well as π bonded Fe atoms, which was confirmed by X-ray structure determination. The second reaction resulting in the formation of bimetallic dithiolato complex **29** involves insertion of two iron atoms in the sulfur-sulfur bond of the intermediate diphenyl dithiirane. The latter is the product of the ring closure of thiobenzophenone *S*-sulfide formed after the initial [3+2]-cycloelimination step[44] (Scheme 26). The formation of complexes of types **28** and **29** was postulated in reactions of substituted thiobenzophenones as well as 3,3,5,5-tetraphenyl-1,2,4-trithiolane (**1b**) with $Fe_2(CO)_9$, but no mechanistic explanation was presented.[45]



Scheme 26. Formation of the bimetallic complexes **28** and **29** in reactions of 3,3,5,5-tetraphenyl 1,2,4-trithiolane (**1b**) with $Fe_2(CO)_9$.

5. Conclusions

The present review summarizes the most important aspects of the organic and organometallic chemistry of 1,2,4-trithiolanes, which form a relevant class of non-aromatic sulfur-rich heterocycles and updates our earlier article related to similar problems.[46] Some of them are abounded in nature and are important components of fragrances and food-stuff. They are of practical importance for the synthesis of other sulfur containing heterocycles via [3+2]-cycloaddition of the *in situ* generated thiocarbonyl*S*-sulfides acting as reactive 1,3-dipoles. The latter are believed to exist in equilibrium with corresponding dithiiranes. In addition, 1,2,4-trithiolanes easily react with electron-rich, low-valent platinum(0) complexes of type $L_2Pt(0)(\eta^2\text{-olefin})$ (L = phosphanes) yielding platinathiiranes and dithiolato platinum(II)

complexes, respectively. Formation of dithiolato platinum(II) complexes results from the oxidative addition of $L_2Pt(0)(\eta^2$-olefin) along the sulfur-sulfur bond of the elusive dithiirane derivatives. Similar processes govern reactions of 1,2,4-trithiolanes with iron carbonyls $Fe_2(CO)_9$ and $Fe_3(CO)_{12}$ leading to iron-sulfur clusters which are of great current interest.[47] Some of them are considered as [FeFe]-hydrogenase mimics of potential importance for electro- and photocatalytic production of hydrogen.[48]

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Keywords:1,2,4-trithiolanes, [3+2]-cycloaddition, flash vacuum pyrolysis, platinathiiranes, dithiolato complexes

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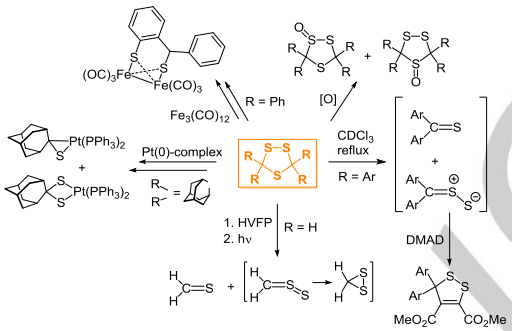
Layout 1:

MINIREVIEW

1,2,4-Trithiolanes belong to the class of cyclic polysulfides and some of them are abundant in nature. Thermal [3+2]-cycloelimination of 1,2,4-trithiolanes leads to the generation of reactive thiocarbonyl *S*-sulfides, which exist in equilibrium with the corresponding dithiiranes. 1,2,4-Trithiolanes react with low valent metals (platinum and iron) forming the corresponding sulfur-metal complexes.

*



Cyclic polysulfides

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Organic and Coordination Chemistry of 1,2,4-Trithiolanes